

CLAIMS

1. A method of identifying an antigen-responsive T cell within a population of T cells, the method comprising the steps of

(1) obtaining a sample containing T cells which have responded to the antigen;

(2) determining <sup>(A) selected species (A)</sup> individually for each of a plurality of specific T cell receptors, <sup>(B)</sup> or individually for each of a plurality of subsets of T cell receptors, whether expression of a gene encoding a specific T cell receptor, or whether expression of genes encoding a subset of T cell receptors <sup>(B)</sup> has increased <sup>(A)</sup> per specific T cell receptor-positive T cell or per specific T cell receptor-positive T cell subset compared to the expression of said gene or genes in a sample containing T cells which have not responded to the antigen.

specific to

selected  
- plurality of TCR  
- specific TCR  
- per specific TCR  
(B)  
- subsets of TCR  
- specific subsets  
- per TCR subset

2. A method according to Claim 1 of identifying an antigen-responsive T cell within a population of T cells, the method comprising the steps of

(1) obtaining a sample containing T cells which have responded to the antigen;

(2) determining <sup>(A)</sup> individually for each of a plurality of specific T cell receptors, <sup>(B)</sup> or individually for each of a plurality of subsets of T cell receptors, the amount of T cell receptor

mRNA, which mRNA is specific for a T cell receptor or is specific for a subset of T cell receptors, per specific T cell receptor-positive T cell or per specific T cell receptor-positive T cell subset, in the sample obtained in step (1);

and

- (3) determining which T cell receptor mRNA has an increased amount per specific T cell in the sample obtained in step (1) compared to that in a sample containing T cells which have not responded to the antigen.

3. A method according to Claim 2 wherein step (1) comprises obtaining (a) a sample containing T cells which have not responded to the antigen and (b) a sample containing T cells which have responded to the antigen and in step (3) it is determined which T cell receptor mRNA has an increased amount per specific T cell in sample (b) compared to sample (a).

4. A method according to Claim 3 wherein sample (a) is obtained from a non-diseased site of an individual and sample (b) is obtained from a diseased site of the individual.

5. A method according to Claim 3 wherein sample (a) is obtained from a non-diseased individual and sample (b) is obtained from a diseased individual.

Not  
selected

selected

6. A method according to any one of Claims 1 to 5 wherein the subset of T cell receptors is a subset wherein each T cell receptor comprises a specific V $\beta$  region.  
*Not clear*
- 5 7. A method according to any one of Claims 1 to 5 wherein the subset of T cell receptors is a subset wherein each T cell receptor comprises a specific V $\alpha$  region.  
*maybe even*
8. A method according to any one of the preceding claims wherein the subset of T cell receptors is a subset wherein each T cell receptor comprises a specific V $\alpha$  and a specific V $\beta$  region.  
*No*
- 10 9. A method according to Claim 8 wherein the subset of T cell receptors is a subset wherein each T cell receptor comprises a specific J region.
- 15 10. A method according to any one of Claims 2 to 9 wherein the amount of T cell receptor mRNA is determined using quantitative PCR.
- 20 11. A method according to Claim 10 wherein the quantitative PCR is reverse-transcription-competitive PCR (RT-CPCR).
- 25 12. A method according to any one of the preceding claims wherein the number of specific T cell receptor-positive T cells or the number of T cell receptor-positive T cells in a specific subset is determined using antibodies which bind to a specific T cell receptor or to a specific subset of T cell receptors.  
*Not clear*

13. A method according to Claim 12 wherein the antibody is an anti-specific V $\beta$  region antibody. *Not a claim*
14. A method according to Claim 12 wherein the antibody is an anti-specific V $\alpha$  region antibody.
15. A method according to any one of Claims 1 to 11 wherein the number of specific T cell receptor-positive T cells or the number of T cell receptor-positive T cells in a specific subset is determined by quantifying the amount of specific T cell receptor DNA, or the amount of T cell receptor DNA in a specific subset, in the samples obtained in step (1).
16. A method according to Claim 15 wherein the amount of specific DNA is determined using quantitative PCR.
17. A method according to Claim 16 wherein the quantitative PCR is competitive PCR.
18. A method of treating a patient with an antigen-mediated disease the method comprising (a) identifying an antigen-responsive T cell associated with an antigen-mediated disease according to the method of Claim 1 and (b) administering to the patient an effective amount of an agent selected to ameliorate the disease.
19. A method according to Claim 18 wherein the agent reduces or eliminates the T cell response to the antigen.

20. A method according to Claim 18 or 19 wherein the method comprises T cell vaccination or anti-TCR antibody treatment or peptide immunization.